REMARKS

Review and reconsideration of the above-identified application and claims in view of Applicants' following remarks are respectfully requested. Claims 1-14 are pending.

Claims 1-14 were rejected under 35 U.S.C. §103(a) over Gilmanshin et al. in view of Cubicciotti, and further in view of Schwartz et al. The Office Action states that it would be obvious to substitute a method of using two or more optically distinguishable DNA sequence recognition units (Schwartz et al.) into a method for single molecule identification of a target DNA molecule in a random coil state as taught by Gilmanshin et al. in view of Cubicciotti. For at least the following reasons, reconsideration and withdrawal of the rejection are in order.

The invention is directed to a means of identifying an unknown target DNA molecule by optical visualization of the location of tagged, known sequences of nucleotides attached to the target. Optically distinguishable materials are attached to DNA sequence recognition units that have a known nucleotide sequence. The resulting optically distinguishable DNA sequence recognition units are then added to an unknown target, wherein the sequence recognition units hybridize to the target. The target is stretched to a substantially linear configuration, and the order of the optically distinguishable materials is identified under a microscope. The order in which the optically distinguishable materials are observed indicates the nucleotide sequence of the target, because the nucleotide sequence of each DNA sequence recognition unit attached to an optically distinguishable material is known. In this manner, known sequences within an unknown target can be identified using a library of known, uniquely tagged DNA sequence recognition units. *See*, for example, Figure 1 of the application, and the specification at least at page 4, line 31, - page 5, line 10, and page 7, lines 15-28.

In contrast, as discussed in the response filed June 18, 2003, Gilmanshin et al. does not use an optically distinguishable material as a label. Gilmanshin et al. detects a unit specific marker identifying a polymer by identification of an object-dependent impulse, such as a light signal, generated by an interaction between the unit-specific marker on the polymer and a station. The unit-specific marker is not visually detectable by itself. Instead, it is a fluorescent dye, groove binder, intercalator, protein, or other like object that is observable only upon interaction with a station (*see*

col. 8, lines 44-55), wherein a station may be a bead (*see* Fig. 5B and column 24, line 61, to column 26, line 3). Gilmanshin et al. does not disclose or suggest the use of an optically distinguishable material, requiring instead interaction of a label and a station for identification. Further, Gilmanshin et al. does not disclose an optically distinguishable material of about 0.05 μm or greater, as admitted in the Office Action. Gilmanshin et al. does not identify a single molecule of a target DNA molecule by detecting two or more optically distinguishable DNA sequence recognition units, wherein the DNA sequence of the recognition units is known.

Cubicciotti does not overcome the deficiencies of Gilmanshin et al. Cubicciotti is directed to a method of identifying a single, unknown, nonnaturally occurring oligonucleotide sequence in a library of nonnaturally occurring oligonucleotides of unknown sequence. The method includes labeling a known sequence and adding it to the library, where the known sequence covalently attaches or hybridizes to the desired target, if present. The target/sequence complex is identified by its physical properties by means of scanning probe microscopy, optical trapping, or flow cytometry. As a reporter for identifying the nonnaturally occurring sequence from the library, a nanosphere with a diameter of 10-300 nm can be used. *See*, for example, Example 22, col. 247, lines 1-13. Cubicciotti does not disclose or suggest the use of two or more optically distinguishable materials attached to respective known DNA sequence recognition units to identify a single molecule of a target DNA molecule, as claimed by Applicants, and therefore does not overcome the deficiencies of Gilmanshin et al.

Schwartz et al. does not overcome the deficiencies of Gilmanshin et al and Cubicciotti. Schwartz et al. discloses a method of identifying a DNA sequence by stretching a target DNA strand, attaching it to a substrate, nicking the strand in one or more locations, and incorporating an individual labeled nucleotide into the target at each nicked site. The order of the incorporated labeled nucleotides can be determined to aid in sequencing the target. Schwartz et al. does not disclose or suggest the use of two or more optically distinguishable materials attached to respective known DNA sequence recognition units to identify a single molecule of a target DNA molecule, as claimed by Applicants, and therefore does not overcome the deficiencies of Gilmanshin et al. or Cubicciotti.

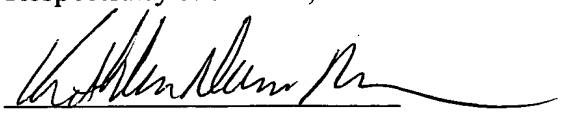
As stated above, the cited references are directed to identification of a polymer sequence by identification of an object-dependent impulse (Gilmanshin et al.), identification and removal of an unknown target oligonucleotide sequence from a library of sequences (Cubicciotti), and determination of a DNA sequence by incorporating labeled nucleotides into an unknown sequence (Schwartz et al.). All of these methods pertain to sequencing an unknown target or identifying an unknown target from a collection of targets. In contrast, the claimed invention relates to identification of a single molecule by observing the location of two or more known sequences within a target, wherein the location of each known sequence in the target DNA molecule can be determined by observation of the optically distinguishable sequence recognition units marking each known sequence attached to the target. None of the references, alone or in combination, disclose or suggest a means of single molecule identification of a target DNA molecule by optical identification of the location of two or more known sequences within the target DNA molecule.

Further, one of ordinary skill in the art would not seek to combine the references. The use of the reporters of Cubicciotti in the process of Gilmanshin et al., as suggested in the Office Action, would not result in identification of a nucleic acid sequence, as taught by Gilmanshin et al., because the reporter of Cubicciotti cannot be identified by the bead matrix of Gilmanshin et al. without substantial modification to the process. Similarly, the labeled nucleotide of Schwartz et al. cannot be identified by the process of Gilmanshin et al. or Cubicciotti, because Schwartz et al. incorporates the labeled nucleotide into the DNA sequence. The unit specific marker of Gilmanshin et al. cannot function in the methods of Cubicciotti or Schwartz et al. without substantial modification of the methods. There is no motivation to combine the references because any such combination would defeat the purpose of and/or make inoperative the process of one or more other references.

In view of the above remarks, reconsideration and withdrawal of the rejection of claims 1-14 under 35 U.S.C. §103(a) over Gilmanshin et al. in view of Cubicciotti, and further in view of Schwartz et al., are in order.

For at least the reasons set forth above, Applicants submit all of Claims 1-14 are in condition for allowance. Prompt and favorable action is respectfully requested. Should the Examiner require anything further, he is invited to contact Applicants' undersigned representative.

Respectfully submitted,



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